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Effects of theta burst stimulation over the dorsolateral prefrontal cortex on language switching – A behavioral and ERP study

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ABSTRACT

This study investigated the role of the left dorsolateral prefrontal cortex (DLPFC) in language switching using theta burst stimulation (TBS) and electroencephalography in late bilinguals. After a sham-controlled baseline, participants received either excitatory or inhibitory TBS over the left DLPFC before conducting picture naming tasks in pure language blocks and a language switching block, as well as a nonverbal switching task. On the behavioral level, we found no effect of TBS. However, the ERP-analysis revealed an effect of *Stimulation* for the picture naming tasks, characterized by alterations in the left DLPFC at 20–72 ms, and in networks associated with conflict resolution and self-monitoring at 533–600 ms. As we did not find an interaction between *Stimulation* and *Block* (switching vs non-switching), prefrontal stimulation did not specifically modulate inter-language control. The left DLPFC might rather be involved in enhancing maintenance of task demands and self-monitoring during language production in both mono- and bilingual contexts.

1. Introduction

The way bilinguals are able to restrict their speech to one language or intentionally switch languages according to contextual cues remains an intriguing question. The present study aims at exploring the functional relation between the left dorsolateral prefrontal cortex (DLPFC) and the ability to switch between languages in healthy late bilinguals using theta burst stimulation (TBS) and electroencephalography (EEG).

Most present models of bilingual language control assume that when selecting words in one language, the lexical nodes of both languages can receive activation from the semantic system (Bobb & Wodniecka, 2013; Colomé, 2001; Declerck & Philipp, 2015). According to these language-unspecific selection models, the activation of the non-target language nodes needs to be suppressed when switching to the target language (Abutalebi & Green, 2008; Yi, Chen, Chang, Wang, & Wu, 2018). To suppress the interference of the non-target language, it has been speculated that bilinguals recruit executive control regions including the left DLPFC, anterior cingulate cortex (ACC), inferior parietal lobule and basal ganglia (Abutalebi & Green, 2008; Hervais-Adelman, Moser-Mercer, & Golestani, 2011). Left frontal and bilateral subcortical regions have also been reported to be active during language switching as compared to monolingual tasks in a quantitative meta-analysis by Luk, Green, Abutalebi, and Grady (2012). Neuropsychological cases (Fabbro, Skrap, & Aglioti, 2000; Meuter, Humphreys, & Rumiati, 2002; Nardone et al., 2011) as well as neuroimaging (Hernandez, Dapretto, Mazziotta, & Bookheimer, 2001; Hernandez, Martinez, & Kohnert, 2000; Khateb et al., 2007; Mouthon et al., 2019) and intracranial electric stimulation studies (Lubrano, Prod'homme, Démonet, & Köpke, 2012; Sierpowska et al., 2018, 2013) assume a causal role of the left DLPFC in language control. However, two case studies investigating noninvasive brain stimulation (NIBS) over the left frontal cortex showed deviating effects on language switching (increase versus decrease after excitatory stimulation; Holtzheimer, Fawaz, Wilson, & Avery, 2005; Nardone et al., 2011). Moreover, no study has so far investigated whether the left DLPFC specifically contributes to inhibiting the non-target language. Colzato et al. (2008) suggested that rather than directly reducing activation of the non-target language, the left DLPFC might induce an increase of activation of the target language by efficient top-down attentional control during language switching. This higher activation would then, as a side effect, lead to a reactive inhibition of the non-target language. Yet this causal link between attentional control and reactive inhibition

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has not been empirically confirmed so far. In contrast, a language switching study using magnetoencephalography (MEG) found a specific increase of activity in the DLPFC during *dis*engagement from the previous language (Blanco-Elorrieta, Emmorey, & Pylkkänen, 2018), as such specifying how the DLPFC might enhance cognitive flexibility in the control of languages. Hervais-Adelman et al. (2011) suggested two distinct networks contributing to the executive control of language, without specifying to which loop the left DLPFC belongs: a fronto-basal-ganglia loop implicated in the inhibition of inappropriate languages, and a fronto-parietal network that sustains more general switching mechanisms. Following these models, the functional role of the left DLPFC in switching between the mother tongue (L1) and a second language (L2) and whether language switching can be modulated by prefrontal NIBS still remain inconclusive.

Here, we present a study investigating the effects of NIBS over the left DLPFC on language switching and its neuronal correlates in a sham-controlled, single blind group study including 40 healthy late bilinguals (L1 German, L2 English). We compared the effect of intermittent theta burst stimulation (iTBS) vs continuous theta burst stimulation (cTBS) and included a sham-controlled baseline. TBS is a repetitive transcranial magnetic stimulation (rTMS) protocol that has previously been shown to be effective in modulating prefrontal cortical excitability (Lowe, Manocchio, Safati, & Hall, 2018).

The primary aim of the current study was to investigate whether prefrontal NIBS can modulate language switching. As our main hypothesis, we expected higher response times (RTs) after inhibitory TBS (i.e. cTBS) as compared to excitatory TBS (i.e. iTBS) over the left DLPFC, with stronger effects for language switching blocks as compared to pure language blocks. Assuming that the left DLPFC belongs to the network implicated in general language switching (Blanco-Elorrieta et al., 2018; Hervais-Adelman et al., 2011), inhibition of the DLPFC would impair, while excitation would enhance switching abilities. Alternatively, if the left DLPFC belongs to the network implicated in the inhibition of non-target languages, exciting the DLPFC could lead to an increase in inhibition and therefore to an increase in RTs in the language switching blocks, whereas inhibiting the DLPFC would lead to the opposite pattern.

As a second aim, we explored the electrophysiological correlates of prefrontal neuromodulation by iTBS vs cTBS and its interaction with the language-switching pattern using event-related potentials (ERPs). Adding an ERP analysis allowed us to better assess the impact of prefrontal stimulation on the temporal dynamics of language control. Using global ERP analyses, we investigated (1) how and when prefrontal iTBS vs cTBS changes brain activity during verbal language production (main effect of *Stimulation*), and (2) whether these changes are specifically observed during the suppression of the non-target language (interaction between *Stimulation*, *Language* and *Block*).

As a subsidiary aim, we investigated whether possible effects of prefrontal NIBS are specific to language, or rather associated with a domain-general executive control modulation. As such, we also included a nonverbal switching task. Assuming that the DLPFC could be essential both for language and nonverbal switching (Dove, Pollmann, Schubert, Wiggins, & Yves von Cramon, 2000), we expected an increase of RTs following cTBS as compared to iTBS in both tasks.

2. Material and methods

2.1. Declaration of ethical approval

All participants gave written informed consent prior to participation. The study was approved by the local Competent Ethics Committee and preregistered on "clinicaltrials.gov" (NCT03148470).

2.2. Participants

41 healthy late bilinguals (31 women, mean age = 22.4 ± 4.2 years) participated in the study. All participants were native German/Swiss-German speakers (L1), learned English (L2) after the age of seven (mean Age of Acquisition = 11.35 ± 1.85) and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). None of the participants reported any history of neurological or psychiatric illness, intracranial metal, cochlear implant or pacemaker. One participant was excluded from the study as he reported light nausea during iTBS, resulting in an immediate stop of the stimulation after two minutes. The reported nausea diminished within 30 min after stimulation. The final group for the behavioral analysis included 20 participants in the cTBS group (16 women, mean age = 22.8 ± 5.36) and 20 participants in the iTBS group (15 women, mean age = 22.1 ± 2.7).

2.3. Language evaluation

For the assessment of language background and immersion, participants filled out a custom-made questionnaire (Buetler et al., 2015; Wartenburger et al., 2003) asking for the age of acquisition and the presence of L2 in current daily-life activities. To evaluate L2 vocabulary, a sub-test from the computer-based DIALANG language diagnosis system was performed (Zhang & Thompson, 2004). For the self-evaluation part, participants rated their L2-skills (speaking, understanding, reading and writing) on a 10 cm scale ranging from "no mastering" (0) to "perfect mastering" (10). As can be seen in Table 1, participants in the two experimental groups had comparable L2 language skills and only differed in their self-evaluation of writing skills, with higher self-rated writing skills by the cTBS compared to the iTBS group.

2.4. Experimental procedure

The whole experimental procedure is depicted in Fig. 1. As a baseline-measure, all participants received sham-TBS immediately before conducting the following tasks: (1) a block of picture naming in L1 only, (2) a block of picture naming in L2 only, (3) a language switching block with picture naming alternated between L1 and L2, and (4) a nonverbal switching task. After a 10 min break, half of the participants received iTBS and the other half cTBS over the left DLPFC immediately before conducting parallel versions of the same tasks described above. Participants were blind towards all stimulation conditions. To familiarize participants with the words used in the picture-naming tasks and to homogenize familiarity with the stimuli across groups, they saw each image on a screen and were orally presented to the corresponding word in L1 and L2. The familiarization for the pictures/words used in the sham-condition was done immediately before applying the sham-stimulation, and the familiarization for the pictures/words used in the TBS-condition (iTBS/cTBS) was done immediately prior to the iTBS/cTBS stimulation. The order of tasks was counterbalanced across participants.

2.5. Theta burst stimulation

Both iTBS and cTBS were applied using a MagPro X100 stimulator connected to a MCF-B70 Butterfly Coil. For the sham stimulation, we used a MCF-P-B70 placebo coil. TBS was delivered at 80% of participants' individual resting motor threshold (MT) and applied over F3, overlying the left DLPFC according to the International 10–20 EEG system (Herwig, Satrapi, & Schönfeldt-Lecuona, 2003), with the handle pointing posteriorly. MT and stimulation were applied with the EEG cap placed on the head without cables attached. To determine the resting MT, the handle was positioned 45° backwards with respect to the head's midline over the left primary motor cortex (M1). MT was defined as the minimum stimulator output that evoked observable small hand muscle twitches in the right relaxed hand in at least 5 out of 10 trials (Pridmore, Fernandes Filho, Nahas, Liberatos, & George, 1998).

During iTBS, a two second train of TBS (10 bursts of three pulses at

Table 1
Language Assessment of L2 (English).

Immersion:	cTBS (n = 20) % of L2 use in daily-life					iTBS (n = 20) % of L2 use in daily-life					Group differences[1]	
	0%	25%	50%	75%	100%	0%	25%	50%	75%	100%		
Use of English at work (n)	10	10	0	0	0	11	9	0	0	0		
Use of English with friends (n)	11	6	3	0	0	12	6	2	0	0		
Use of English in media (n)	0	9	7	3	1	2	9	2	5	2		
Use of English when reading (n)	3	8	7	2	0	3	14	2	1	0		
	Mean ± SD					**Mean ± SD**					***t***	***p***
English AoA	11.25 ± 2.2					11.25 ± 2.2					−0.34	0.737
Self evaluation[2]:												
Speaking	7.1 ± 1.4					6.6 ± 1.6					1.063	0.294
Understanding	7.7 ± 1.3					7.5 ± 1					0.616	0.541
Reading	7.8 ± 1.1					7.5 ± 1.4					0.987	0.33
Writing	6.5 ± 1.3					5.4 ± 1.7					2.366	0.023*
Dialang[3]:												
Score	792.3 ± 135.3					752 ± 168.5					0.833	0.41

Abbreviations: cTBS = continuous theta burst stimulation group; iTBS = intermittent theta burst stimulation group; n = number of participants; AoA = Age of Acquisition

[1] Group differences assessed with independent *t*-tests. Significance codes:'*' < 0.05.

[2] Self evaluation measured on a 10 cm scale ranging from 0 (no mastering) to 10 (perfect mastering).

[3] Dialang score: 401–600 = "good basic vocabulary"; 601–900 = "very substantial vocabulary"; 901–1000 = "near-native proficiency".

50 Hz, repeated at intervals of 200 ms) was repeated every 10 s for a total of 190 s (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). This protocol, which includes 600 pulses, has been shown to increase motor cortical excitability for up to 60 min (Wischnewski & Schutter, 2015). cTBS consisted of 801 pulses delivered in 44 s (267 bursts of three pulses at 30 Hz, repeated at intervals of 100 ms), a protocol which has previously been able to induce a consistent inhibitory effect (Nyffeler et al., 2006). In sham stimulation, the same iTBS/cTBS protocols were used with the placebo coil connected to the device. After each experimental session (sham and real TBS), participants rated possible side effects such as headache, neck pain, burning sensation on the skin, prickling sensation on the skin, doziness, difficulties in concentrating or change in mood from 1 (absent) to 4 (severe). The ratings of side effects did not differ between sham and real TBS apart from the experience of a prickling sensation, which was higher for real TBS as compared to sham TBS (p = .036 for iTBS, p = .014 for cTBS, Wilcoxon signed rank tests).

2.6. Tasks and material

Participants were seated in an electrically shielded and sound attenuated booth 120 cm in front of a 22-in. LED screen. Stimuli were presented on a light gray background in the center of the screen. For the picture naming tasks, the language was indicated by a cue (letter D for *Deutsch*, letter E for *English*), which was presented on the computer screen for 500 ms, followed by a fixation cross with a cue-stimulus interval (CSI) of 500–1000 ms. A picture was then presented centrally on the screen for 3000 ms. In the language switching block, the cue alternated predictably after each trial. According to Declerck and Philipp (2015), predictable language switching allows for "language preplanning", as the participants know when switching to another language will occur, which is similar to preplanning during natural language production. Responses were given verbally and were recorded through a microphone. The participants were encouraged to respond as fast as possible while avoiding errors. The stimuli for the picture naming tasks consisted of 180 images from the databases normed in English and German by Bates et al. (2003). Two different sets of 90 images were used for sham TBS and real TBS, with the order counterbalanced between participants. Out of these sets of 90 images, the same 45 images used for L1 in the non-switching block were then also used for L2 in the switching block, and vice versa. The four lists of 45 images were matched in both languages for naming RT, log transformed lemma frequency, concept agreement, visual complexity, word length, number of syllables and number of cognates. Within each list, the English and German words were also matched across languages for naming RT, log-transformed lemma frequency, name agreement and concept agreement (Bates et al., 2003).

In the nonverbal switching task, participants had to switch between a low/high and an odd/even classification of a digit. A cue (" < " for low/high and "/I" for odd/even) was presented in the center of the screen for 500 ms, followed by a fixation cross with a cue-stimulus interval of 500–1000 ms. A digit from the set {1–4, 6–9} was then randomly displayed in 36-pt Arial in the center of the screen. Participants were given 2000 ms to press the left key using their right index finger to classify the digit as being odd or smaller than 5 and the right key using their middle finger to classify the digit as being even or bigger than 5. The cue changed predictably after each trial, with a total of 50 trials (Nessler, Friedman, & Johnson, 2012). As was the case in the language-switching block, participants were encouraged to respond as fast as possible while avoiding errors. All tasks are shown in Fig. 2.

2.7. Behavioral analysis

Each spoken response was checked for accuracy and RT using the software CheckVocal (Protopapas, 2007), which allows for manual adjustments of the RT in case of hesitations, lip smacking or auto-corrections. Synonyms of words for the target language were defined as correct responses (e.g. "gift" for the target word "present"). Only correct responses were included in the RT analysis.

Analyses were conducted using mixed-effects models with crossed random effects for participants and items using the packages lme4 (Version 1.1–17, Bates, Mächler, Bolker, & Walker, 2014) and lmerTest (Version 3.0–1) of R (Version 3.5.0, R Core Team, 2018). As visual inspection of the residual plots revealed heteroscedasticity in all tasks, we log-transformed the RT data. The analysis for the picture naming tasks included contrast coded fixed effects for *Stimulation* (−0.5 = iTBS, 0.5 = cTBS), *Language* (−0.5 = L1, 0.5 = L2), and *Block* (−0.5 = Non-Switching, 0.5 = Switching) in a 2 × 2 × 2 factorial design. Random effects were fit using a maximal random effects structure (Barr, Levy, Scheepers, & Tily, 2013), which included random intercepts for participants and items and by-participant random slopes for *Language*, *Block* and their interaction.

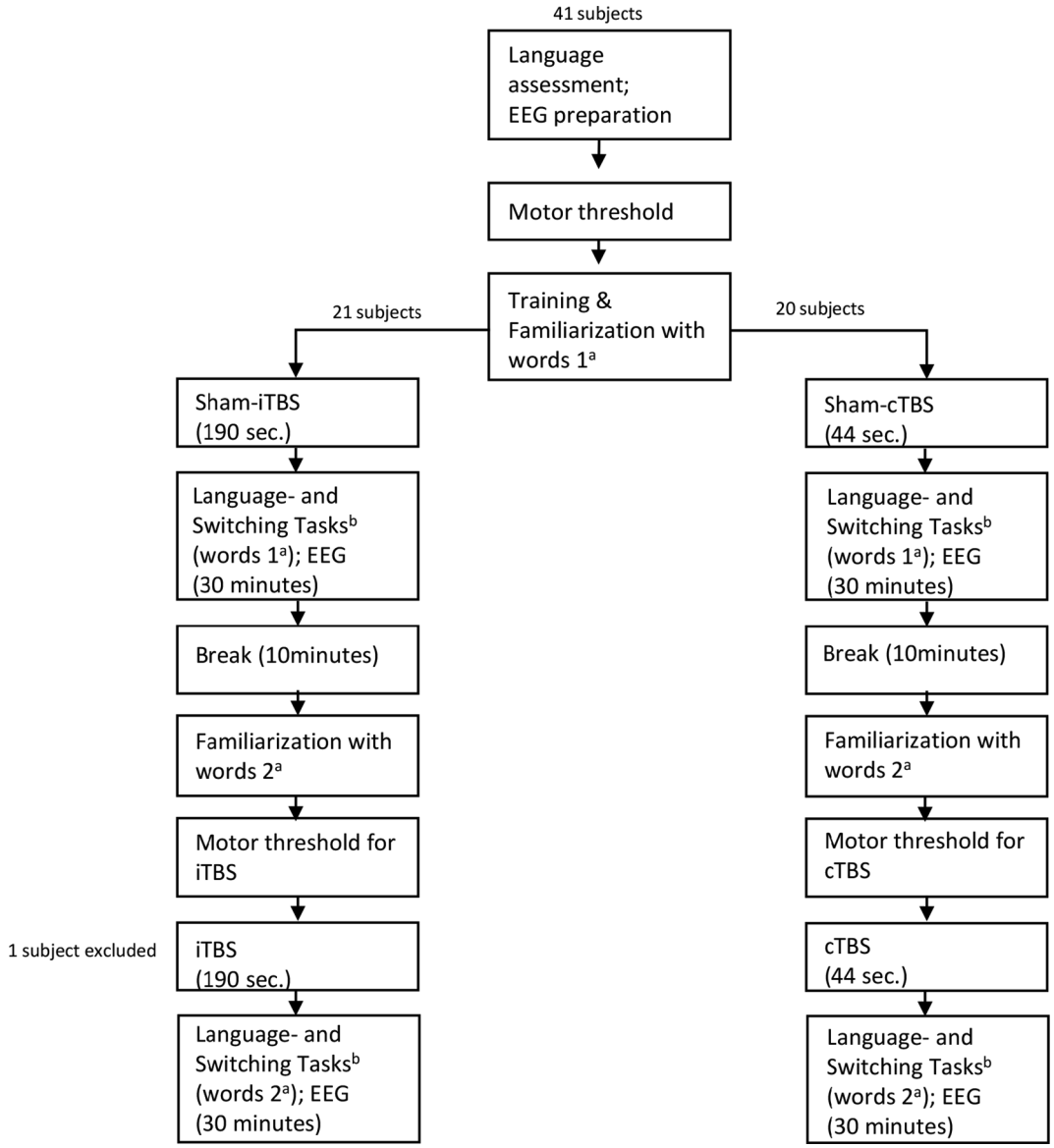

Fig. 1. Procedure of the experiment. [a]Order of words/pictures used in the tasks (words 1 and words 2) counterbalanced between participants [b]Order of tasks counterbalanced between participants.

For the nonverbal switching task, we included the fixed effects *Stimulation* (−0.5 = iTBS, 0.5 = cTBS) and *Classification* (even/odd-classification = −0.5, size classification = 0.5) in a 2 × 2 factorial design. As the numbers were used repeatedly within each condition, we used random intercepts for participants and numbers, by-participant random slopes for *Classification* as well as by-number random slopes for *Classification*, *Stimulation* and their interaction.

To compare TBS with sham-TBS both for the comparison of iTBS vs sham-iTBS and cTBS vs sham-cTBS, we computed analyses using fixed effects for *Stimulation* (−0.5 = sham-TBS, 0.5 = real TBS), *Language* (−0.5 = L1, 0.5 = L2), and *Block* (−0.5 = Non-Switching, 0.5 = Switching), random intercepts for participants and items, and by-participant random slopes for *Language*, *Block*, *Stimulation* and their interaction. For the nonverbal switching task, *Stimulation* (−0.5 = sham-TBS, 0.5 = real TBS) and *Classification* (even/odd-classification = −0.5, size classification = 0.5) were used as fixed factors. With a maximal random effects structure, we additionally used random intercepts for participants and numbers, as well as both by-participant ad by-number random slopes for *Classification*, *Stimulation* and their interaction.

2.8. Electrophysiological recording and data preprocessing

EEG was recorded at a sampling rate of 1024 Hz with a 64-channel EEG (Biosemi ActiveTwo system, Amsterdam, Netherlands). EEG data preprocessing was performed offline using the Cartool software (Brunet, Murray, & Michel, 2011). EEG epochs from 100 ms pre-stimulus to 600 ms post-stimulus onset were extracted from the raw EEG, excluding triggers with RTs > 3SD above the mean and RTs < 600 ms in the picture naming tasks to avoid motor artifacts. Data were band-pass filtered (1–40 Hz), notch filtered at 50 Hz and recalculated against the average reference. Event-related potentials (ERPs) were calculated by averaging the extracted epochs separately for each condition. As we focused on the differences between iTBS and cTBS, we did not analyze the ERPs of the sham-conditions for the present paper. Bad channels were interpolated before group averaging. For each participant, the same channels were interpolated across all conditions of the picture naming tasks (mean = 4.3 interpolated electrodes) or for the nonverbal switching task (mean = 2.5 interpolated electrodes). We had to exclude 4 participants in the picture naming tasks and 9 in the nonverbal switching task due to a low number (< 20) of artifact-free

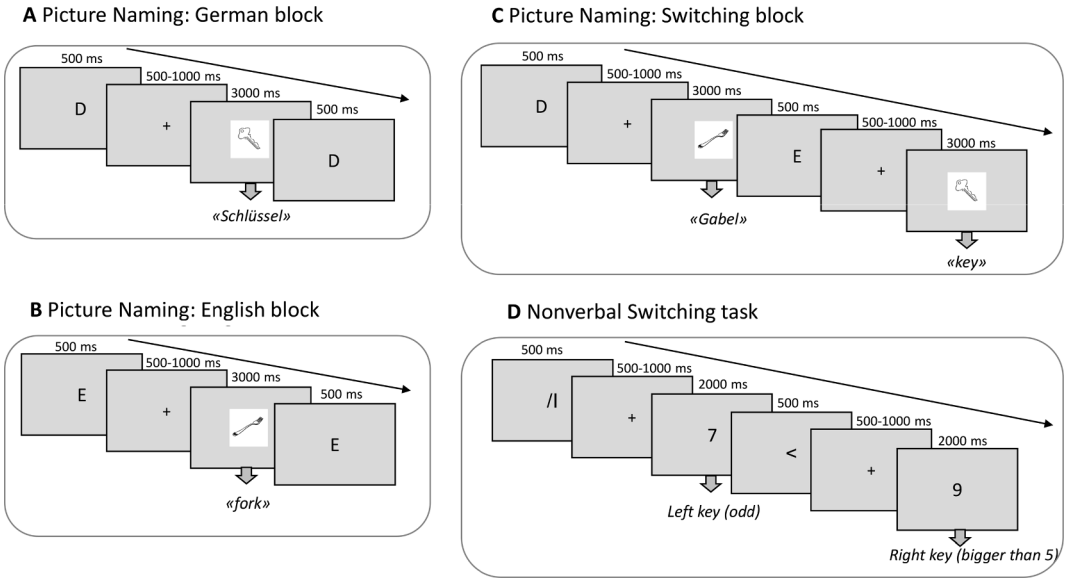

Fig. 2. Picture naming and nonverbal switching tasks.

correct trials. The final group for the ERP analyses thus included 36 participants for the picture naming tasks (19 iTBS; 17 cTBS) and 31 participants for the nonverbal switching task (16 iTBS, 15 cTBS). The average number of accepted epochs was 34.5 ± 5.1 for the picture naming tasks and 37.8 ± 7.5 for the nonverbal task.

2.9. Electrical neuroimaging analysis

We applied a global electric field analysis by comparing the ERPs between conditions across the whole electrode montage, which has been done in a number of studies (Buetler et al., 2015; Hartmann, Wachtl, de Lucia, & Spierer, 2019; Jost, Radman, Buetler, & Annoni, 2018; Maurer, Blau, Yoncheva, & McCandliss, 2010). This approach has the advantage of being reference-independent, allowing to differentiate between differences in response strength and differences in topography, which reflects differences in the configuration of the underlying brain sources (Michel et al., 2004; Tivadar & Murray, 2018; Tzovara, Murray, Michel, & De Lucia, 2012). A standard assumption in the group analysis of ERPs is that within a defined experimental condition, the subjects activate common processing resources (Habermann, Weusmann, Stein, & Koenig, 2018). In order to determine if the experimental conditions elicited a consistent neural activation across subjects within conditions, we conducted a topographic consistency test (TCT). Differences in response strength were then assessed by non-parametric randomization tests on the global field power (GFP) (Koenig, Kottlow, Stein, & Melie-García, 2011). The GFP represents the spatial standard deviation of the electric field at the scalp and equals the root mean square across all recording electrodes (Lehmann & Skrandies, 1980). Differences in topography were assessed by a point-to-point topographic analysis of variance (TANOVA). TANOVA is based on the global map dissimilarity calculated as the root mean square of the difference between the strength-normalized voltage potentials across the electrode montage (Koenig et al., 2011; Tivadar & Murray, 2018). TANOVA was conducted on the normalized data, which allows attributing topographic differences to differences in source distribution, and not source strength (Grieder et al., 2012). Both GFP and TANOVA were applied across all participants with a *p*-threshold of 0.05. For the nonverbal switching task, the between-subject factor *Stimulation* (iTBS, cTBS) was used. For the picture naming tasks, the between-subject factor *Stimulation* (iTBS, cTBS) and the within-subject factors *Language* (L1, L2) and *Block* (Switching, Non-Switching) were applied.

In a second step, electrical source estimations were calculated over the time periods showing a significant topographic difference in the TANOVA using a local autoregressive average (LAURA) distributed linear inverse solution (Grave de Peralta Menendez, Gonzalez Andino, Lantz, Michel, & Landis, 2001; Grave de Peralta, González-Andino, & Gómez-González, 2004). The periods of interest were time-averaged for each participant and condition. From the resulting one-time sample ERPs, intracranial sources were estimated and their current density compared at each solution point using ANOVAs. For the ANOVAs, we used the between-subject factor *Stimulation* for the nonverbal switching task, and the between-subject factor *Stimulation* as well as the within-subject factors *Block* and *Language* for the picture naming tasks. The solution space was calculated on a realistic head model including 4928 nodes, selected from a 6.7 mm × 6.7 mm × 6.7 mm grid of voxels equally distributed within the gray matter of the average brain of the Montreal Neurological Institute (MNI). A spatial correction for multiple tests was achieved by considering only clusters of p values < 0.05 with a spatial-extend criterion (k_E) of > 20 contiguous nodes.

3. Results

3.1. Behavioral results

Results of the linear mixed-effects models with the between-subject factor *Stimulation* (iTBS vs cTBS) are presented in Table 2.

For the picture naming tasks, participants were significantly faster in naming pictures in L1 (Mean RT = 1098.82) than L2 (Mean RT = 1158.91) and faster in the non-switching (Mean RT = 1081.14) as compared to the switching block (Mean RT = 1175.24). A significant interaction between *Language* and *Block* indicated an asymmetrical alternation cost, revealing that alternation costs were only present in L1 (see Fig. 3). No differences between iTBS and cTBS were found (estimate = −0.001, p = .932). When compared with the sham-controlled baseline, again no effects of *Stimulation* on RTs were found neither for iTBS (estimate = 0.003, p = .593) nor for cTBS (estimate = 0.010, p = .131) (see Fig. 3).

For the nonverbal task, results indicated faster RTs for the size-judgements (Mean RT = 716.29) as compared to the even/odd-judgements (Mean RT = 817.63). RTs did not differ between cTBS and iTBS (estimate = −0.012, p = .642, see Table 2). When compared with the sham-controlled baseline, no effects of *Stimulation* were found for cTBS (estimate = −0.011, p = .432), but participants were faster after iTBS as compared to sham-iTBS (estimate = −0.027, p = .002).

Table 2
Results of the Linear Mixed Models comparing iTBS vs cTBS.

	Fixed effects				*Random effects*	
					By subject	By item
	Estimate	SE	*t-value*	*p*	*SD*	*SD*
Picture Naming Tasks						
Intercept	3.032	0.008	380.110	< 0.001***	0.045	0.045
Stimulation	−0.001	0.014	−0.086	0.932		
Language	0.026	0.007	3.696	< 0.001***	0.040	
Block	0.037	0.005	6.791	< 0.001***	0.029	
Stimulation * Language	−0.010	0.014	−0.735	0.467		
Stimulation * Block	0.008	0.011	0.695	0.491		
Language * Block	−0.070	0.007	−10.048	< 0.001***	0.026	
Stimulation*Language * Block	0.005	0.014	0.341	0.734		
Nonverbal Switching Task						
Intercept	2.855	0.016	176.628	< 0.001***	0.078	0.028
Stimulation	−0.012	0.026	−0.468	0.642		0.017
Classification	−0.061	0.014	−4.326	0.002**	0.031	0.033
Stimulation * Classification	−0.002	0.017	−0.141	0.889		0.017

Note: All factors were coded using contrast coding as follows: *Stimulation* (−0.5 = iTBS, 0.5 = cTBS), *Language* (−0.5 = L1, 0.5 = L2), *Block* (−0.5 = Non-Switching, 0.5 = Switching), *Classification* (−0.5 = even/odd, 0.5 = size). RT data were log-transformed.
Model formula for the picture naming tasks: RT_Log ~ Language*Stimulation*Block + (1 + Language * Block|Participant) + (1|Item).
Model formula for the nonverbal switching task: RT_Log ~ Classification * Stimulation + (1 + Classification|Participant) + (1 + Classification * Stimulation|Number).
Significance codes: < 0.001 '***', < 0.01 '**', < 0.05 '*'.

3.2. Electrophysiological results

3.2.1. Topographic consistency

Results of the topographic consistency test indicated that there is a significant communality across subjects within all conditions for the entire analysis period, except for the time-window from 133 to 158 ms post-stimulus onset.

3.2.2. Global field power analyses

For the picture naming tasks, the GFP analysis revealed significant periods of differences ($p < .05$) for the effect of *Stimulation* (iTBS vs cTBS) from 60 ms to 30 ms pre-stimulus as well as from 544 ms to 590 ms post-stimulus onset. However, these effects did not pass the test of multiple comparisons according to which 73 consecutive significant timeframes can be expected at a chance level of 0.05. Moreover, the larger time-window from 544 to 590 ms post-stimulus onset occurred at the same time as topographic differences, which indicates differences in underlying neural sources (see below). The GFP analysis did not reveal any significant interactions of *Stimulation* with *Language* and *Block*.

In the nonverbal task, no significant periods of differences were found for the effect of *Stimulation* (iTBS vs cTBS).

3.2.3. Global map dissimilarity

As can be seen in Fig. 4b, the global map dissimilarity analysis identified significant differences in the picture naming tasks between iTBS and cTBS from 20 to 72 ms and from 533 to 600 ms post-stimulus onset ($p < .05$). Moreover, an interaction between *Stimulation* and *Language* was significant from 133 to 164 ms post-stimulus onset ($p < .05$). However, this effect coincides with the time-period showing inconsistent neural activations across subjects within conditions in the Topographic Consistency Test (see Section 3.2.1). As such, this effect cannot be firmly attributed to the experimental conditions and will thus not be further interpreted. The 2 × 2 × 2 interaction with *Block* did not reveal any significant results ($p < .05$).

In the nonverbal switching task, no significant periods of differences were found between iTBS and cTBS.

3.2.4. Electrical source estimations

Electrical source analyses were conducted for the main effects of *Stimulation* from 20 to 72 ms and from 533 to 600 ms post-stimulus onset. The significant topographic differences between iTBS and cTBS in the period 20–72 ms were characterized by differences of activation (cTBS > iTBS) within the frontal lobe, with a local maximum in the left DLPFC ($p < .05$, $k_E = 73$). In the period from 533 to 600 ms post-stimulus onset, differences of activation (cTBS > iTBS) were present in a network of cortical and subcortical areas, with local maxima in the left precentral gyrus, temporal lobe, caudate, insula and cingulate ($p < .05$, $k_E = 631$ and $k_E = 40$).

4. Discussion

To our knowledge, this is the first study investigating the effects of NIBS on language switching in a randomized controlled trial. Against our hypotheses, the behavioral results of this study showed no differences between inhibitory and excitatory left DLPFC stimulation on RTs during language and nonverbal switching. Moreover, the effects of iTBS and cTBS on language switching did not differ from sham stimulation, as such confirming that TBS over the left DLPFC did not affect behavioral outcome when switching between languages.

On an electrophysiological level, the source analysis revealed that stimulation affected brain activity in the left DLPFC during the picture naming tasks at 20–72 ms post-stimulus onset, which can be explained by the specific role of the left DLPFC as top-down control function in maintaining task demands (MacDonald, Cohen, Stenger, & Carter, 2000). It has previously been shown that the left DLPFC is selectively involved during preparatory periods in tasks that require maintenance and manipulation of information in working memory (Barch et al., 1997; Brunoni & Vanderhasselt, 2014; MacDonald et al., 2000), which in our study would be the maintenance of the language cue before accessing the lemma in the corresponding language. Moreover, stimulation affected brain activity at 533–600 ms post-stimulus onset. In language switching studies, this time-window (starting around 500 ms) is commonly referred to as the late positive component (LPC) or P600, and found to be associated with cognitive processes of conflict resolution (Martin et al., 2013; Moreno, Federmeier, & Kutas, 2002; Ng, Gonzalez, & Wicha, 2014; Van Der Meij, Cuetos, Carreiras, & Barber, 2011). During this period, the source analysis indicated a change of brain activity in a network of cortical and subcortical areas including

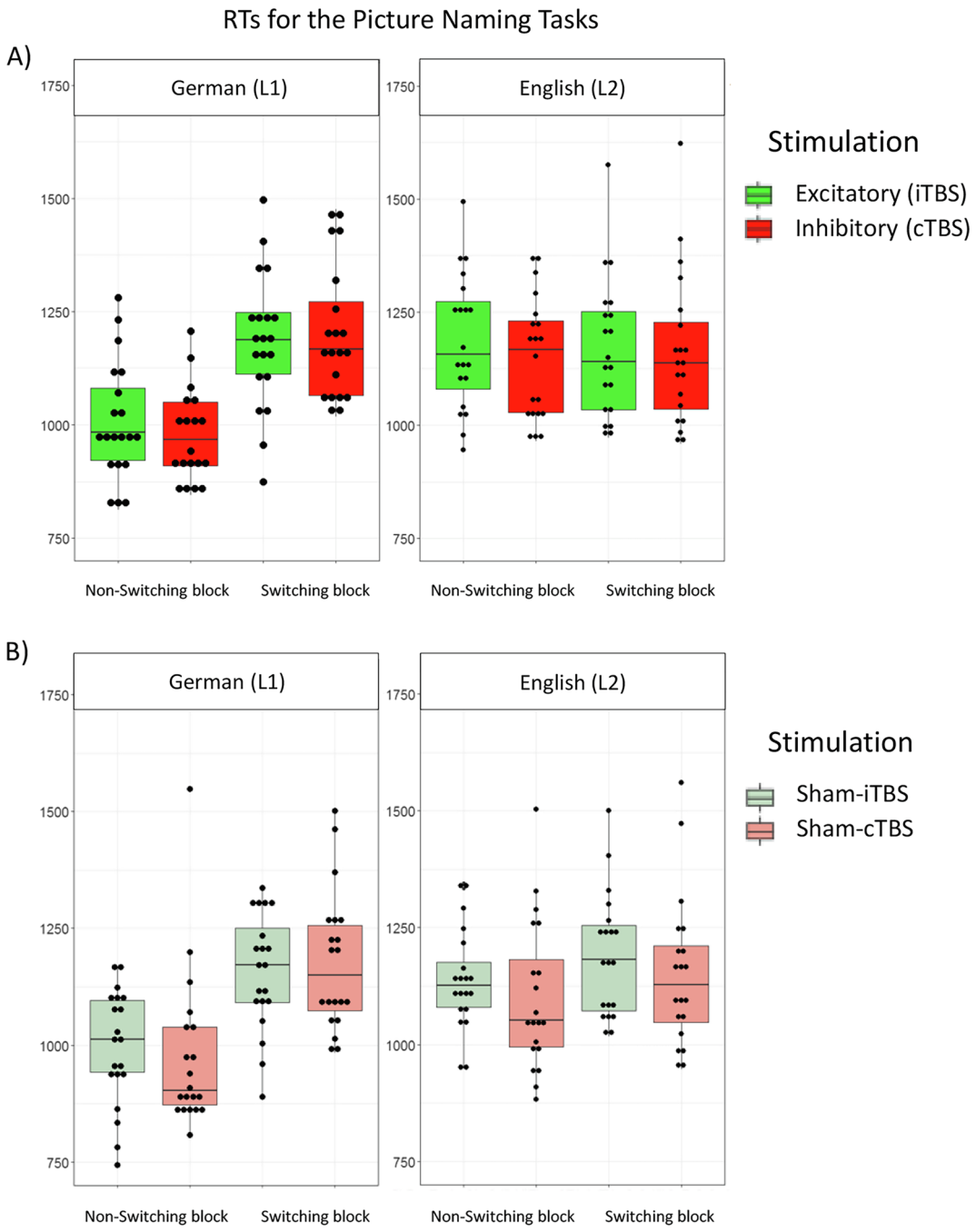

Fig. 3. (A) Response time (RT) data for the picture naming tasks comparing excitatory vs inhibitory TBS. (B) RT data for the picture naming tasks in the sham-controlled baseline.

the cingulate, insula and caudate, which have been associated with executive functions such as conflict resolution and self-monitoring in speech production (Abutalebi & Green, 2016; Indefrey, 2011). These electrophysiological findings are in line with the model of Abutalebi and Green, and consistent with the results reported in a meta-analysis by Luk et al. (2012), suggesting that language control emerges from the interaction of several systems and processes, both at the cortical and subcortical level. The left DLPFC is specifically associated with working memory resources (updating and keeping on-line the relevant language), but also interacts with other cognitive control areas such as the cingulate (Dowdle, Brown, George, & Hanlon, 2018; Tik et al., 2017) and basal ganglia (Casey, Durston, & Fossella, 2001). As we did not find an interaction between *Stimulation* and *Block* (Switching vs Non-Switching), the change of brain activity in these executive control areas following stimulation seems, however, not related to interlanguage control and thus not specifically linked to either switching abilities or a reactive inhibition on a per trial basis (Bobb & Wodniecka, 2013; Colzato et al., 2008). The effect of stimulation might rather reflect an enhancement of top-down attentional control and self-monitoring processes during language production in both mono- and bilingual language modes (Grosjean, 2013). Previous studies using transcranial direct current stimulation (tDCS) to investigate the role of the left DLPFC in picture naming in monolingual (Fertonani, Brambilla, Cotelli, & Miniussi, 2014; Fertonani, Rosini, Cotelli, Rossini, & Miniussi, 2010; Jeon & Han, 2012; Wirth et al., 2011) and bilingual language modes (Radman et al., 2018) have shown mixed results. With TBS, we used a stimulation approach that is more focal in targeting the DLPFC as compared to tDCS (Brunoni & Vanderhasselt, 2014; Miniussi et al.,

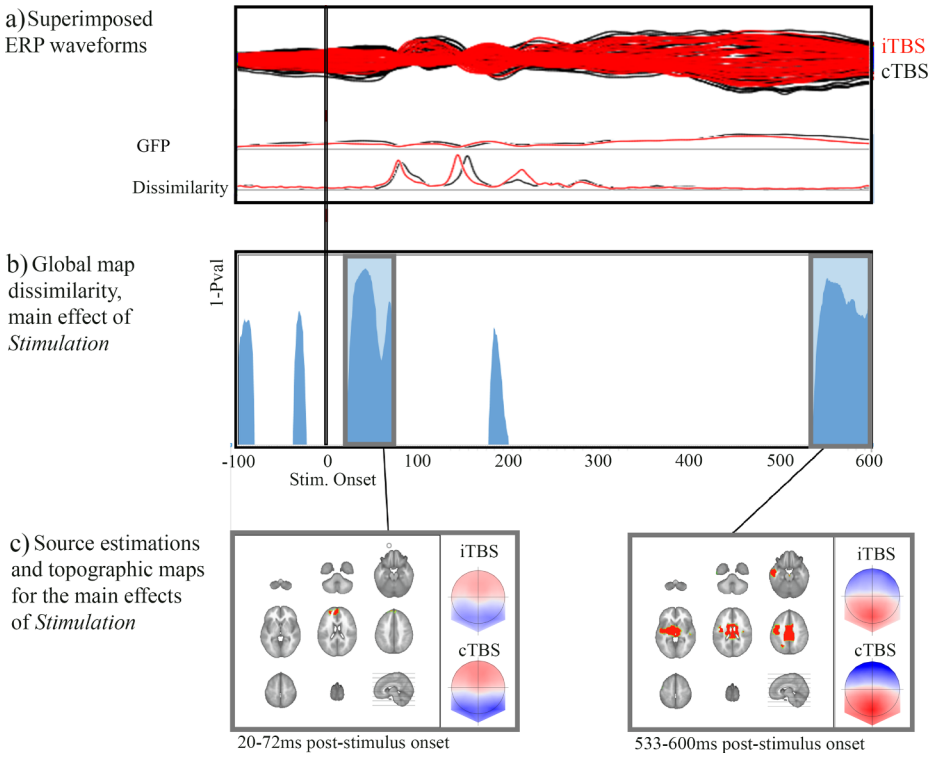

Fig. 4. (a) Superimposed event-related potential (ERP) waveforms, global field power (GFP) and dissimilarity curve for iTBS and cTBS, averaged across *Language* and *Block* across all 64 electrodes. (b) Global map dissimilarity of the main effect of *Stimulation* ($p < .05$), identifying topographic differences between iTBS and cTBS from 20 to 72 ms and 533 to 600 ms post-stimulus onset. (c) Source estimations and topographic maps for the significant time-windows revealing a main effect of *Stimulation* (iTBS vs cTBS).

2008), therefore expanding the knowledge in this field of research. Less activation in all mentioned areas following iTBS as compared to cTBS, is in line with the interpretation that iTBS facilitated performance compared to cTBS in a way that less cognitive resources were needed after iTBS in order to achieve a comparable behavioral performance. We would still like to note here that the source estimations reported should be interpreted cautiously, as the spatial accuracy of EEG inverse solutions, especially for deep sources, is limited and may fail at differentiating between close structures (De Pretto, Rochat, & Spierer, 2017; Grech et al., 2008; Michel et al., 2004). However, applying the conservative statistical approach used in the present paper, this limitation should at least partly be solved.

The electrophysiological effects of stimulation were found only in the picture naming tasks, but not in the nonverbal switching task. Despite several overlapping regions, nonverbal switching, as compared to language switching, has previously been shown to depend more strongly on other regions including left inferior and right superior parietal lobe, left and right superior frontal gyrus and right insula (De Baene, Duyck, Brass, & Carreiras, 2015). It might thus be that the left DLPFC only plays a minor causal role when it comes to nonverbal switching. Though we found a behavioral improvement in nonverbal switching in the iTBS group compared to the sham-controlled baseline, this difference was not significant when comparing iTBS vs cTBS. As we did not include a non-switching block for the nonverbal task, we could not directly compare language vs nonverbal switching in our study. Further studies are needed to directly compare the causal role of the left DLPFC in language vs nonverbal switching, as such specifying the langue vs domain-general cognitive control function of this region.

Independent of stimulation, we observed an asymmetric alternation cost, showing longer RTs for switching vs. non-switching into the more dominant L1 than into L2. This pattern has usually been reported when comparing switching trials vs repetition trials in mixed language blocks, resulting in an asymmetrical switch cost, or when comparing repetition trials from a mixed language block with trials from a pure language block, resulting in a so-called asymmetrical mixing cost (Declerck, 2019, Peeters & Dijkstra, 2018). Although alternative explanations exist (Philipp, Gade, & Koch, 2007; Timmer, Christoffels, & Costa, 2019; Verhoef, Roelofs, & Chwilla, 2009), the asymmetrical switch cost, which has first been described by Meuter and Allport (1999) under the name of "paradoxical" asymmetry in the cost of switching languages, is most commonly explained by the inhibitory control model (ICM) of Green (1998). According to this model, L1 has a higher baseline activation, as it is the more dominant language and used more often than L2. Therefore, when speaking in L1, not much inhibition is required to suppress the less dominant L2. However when speaking in L2, L1 representations must be strongly inhibited to ensure the selection of L2 items. In a language switching block, this inhibition of L1 persists into the following trial. Thus, when switching back to L1, more time is needed to overcome the inhibition of the previous trial, leading to a stronger delay in RTs when switching to L1, but not to the less-dominant L2. As we observed similar patterns as the well-described asymmetrical switch costs, we suggest that the asymmetrical alternation cost in our experiment also represents reactive inhibition on a per trial basis. Alternatively, proactive or sustained inhibition of the nontarget language can better explain asymmetrical mixing costs and could thus also account for the asymmetrical alternation cost found in our study (Declerck, 2019). When naming pictures in a mixed language block, the more dominant L1 might be proactively/sustainedly inhibited to allow for L2 naming, thus leading to more similar levels of L1 and L2 activation in mixed language blocks as compared to single language blocks.

Interestingly, we did not find any interaction between prefrontal stimulation and the asymmetrical alternation cost neither on a behavioral nor on an electrophysiological level. Thus, if the asymmetrical alternation cost represents reactive or proactive inhibition on L1, this inhibition is probably not strongly dependent on activity in the left DLPFC. As such, our finding does also not support the proposed causal link between top-down attentional control and reactive inhibition as described by Colzato et al. (2008). It does, however, support models suggesting different cognitive-control networks to be involved in different processes during language switching, with the DLPFC being specifically involved in top-down modulation of attentional control and working memory (see also Toro, Fox, & Paus, 2008).

To conclude, based on our behavioral and electrophysiological results, it seems that the left DLPFC does not have a direct role in

suppressing the non-target language during language switching, but rather in maintaining task demands and self-monitoring both in mono- and bilingual contexts. In patients with lesions in the DLPFC, a lack of self-monitoring and difficulties in the maintenance of environmental cues in working memory could lead to inappropriate language use and difficulties in switching languages according to contextual changes. However, in healthy bilinguals who have a high level of attentional control and self-monitoring skills, the effects of prefrontal stimulation on language control can only be observed on an electrophysiological level.

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